

IN THE CLAIMS:

Please cancel claims 31, 58 and 59 without prejudice.

Please substitute currently amended claim numbers 30, 32, 33, 34, 37, 38, 39, 40, 41, 42, 43, 44, 45 and 46 for the previously presented claims having the same claim numbers.

1. (canceled)

2. (canceled)

3. (canceled)

4. (canceled)

5. (canceled)

6. (canceled)

7. (canceled)

8. (canceled)

9. (canceled)

10. (canceled)

11. (canceled)

12. (canceled)

13. (canceled)

14. (canceled)

15. (canceled)

16. (canceled)

17. (canceled)

18. (canceled)

19. (canceled)

20. (canceled)

21. (canceled)

22. (canceled)

23. (canceled)

24. (canceled)

25. (canceled)

27. (canceled)

28. (canceled)

29. (canceled)

30. (currently amended) ~~An isolated variant allele of a human kappa opioid receptor gene, comprising a DNA sequence having at least one variation in~~ consisting of SEQ ID NO:1, wherein said variation comprises having one or more substitutions selected from the group consisting of G36T, A843G, C846T, C852T (SEQ ID NO: 2), C948T (SEQ ID NO: 3), ~~or~~ and C1008T (SEQ ID NO: 4), or any combination thereof, wherein the isolated variant is present in patients having an addictive disease.
31. (canceled)
32. (currently amended) The isolated variant ~~allele~~ of Claim ~~31~~ 30, detectably labeled.
33. (currently amended) The isolated variant ~~allele~~ of Claim 32, wherein said detectable label comprises a radioactive element, a chemical ~~which~~ that fluoresces, or an enzyme.
34. (currently amended) An isolated nucleic acid molecule ~~selectively~~ hybridizable to any of the isolated variants ~~allele~~ of Claim ~~31~~ 30 under high stringency hybridization conditions, wherein the nucleic acid molecule is at least 90% homologous with the variant nucleotide sequence.
35. (previously presented) The isolated nucleic acid molecule of Claim 34, detectably labeled.
36. (previously presented) The isolated nucleic acid molecule of Claim 35, wherein said detectable label comprises a radioactive element, a chemical that fluoresces, or an enzyme.
37. (currently amended) A cloning vector comprising the isolated variant ~~allele~~ of a human kappa opioid receptor gene of Claim ~~31~~ 30 and an origin of replication.

38. (currently amended) A cloning vector comprising an origin of replication and an isolated nucleic acid molecule ~~selectively~~ hybridizable to any of the isolated variants allele of a human kappa opioid receptor gene of claim 30 under high stringency hybridization conditions.
39. (currently amended) The cloning vector of either of Claims 37 or 38, wherein said cloning vector ~~comprises of E. coli~~, is selected from the group consisting of a bacteriophages, a plasmids, ~~or~~ and a pUC plasmid or derivatives thereof.
40. (currently amended) The cloning vector of Claim 39, wherein ~~bacteriophages further comprise the bacteriophage is a lambda derivatives- derivative, and wherein the plasmids further comprise plasmid is a pBR322 derivatives derivative, and wherein the pUC plasmid derivatives further comprise derivative~~ is selected from the group consisting of a pGEX ~~vectors- vector~~, ~~or~~ pmal-c, and pFLAG.
41. (currently amended) An expression vector comprising any of the isolated variants of the allele of a human kappa opioid receptor gene of claim 30.
42. (currently amended) An expression vector comprising an isolated nucleic acid molecule ~~selectively~~ hybridizable to any of the isolated variants of the allele of a human kappa opioid receptor gene of claim 30 under high stringency hybridization conditions, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and wherein the nucleic acid molecule is at least 90% homologous with the variant nucleotide sequence.
43. (currently amended) The expression vector of either of Claims 41 or 42, wherein said promoter ~~comprises~~ is selected from the group consisting of immediate early promoters of hCMV, early promoters of SV40, early promoters of adenovirus, early promoters of vaccinia, early promoters of polyoma, late promoters of SV40,

late promoters of adenovirus, late promoters of vaccinia, late promoters of polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC* system, the major operator and promoter regions of phage lambda, control regions of fd coat protein, 3-phosphoglycerate kinase promoter, acid phosphatase promoter, ~~or~~ and promoters of yeast α mating factor.

44. (currently amended) A unicellular host transformed or transfected with an expression vector comprising any of the isolated variants of the allele of a human kappa opioid receptor gene of claim 31 ~~30~~ operatively associated with a promoter.
45. (currently amended) A unicellular host transformed with an expression vector comprising an isolated nucleic acid molecule ~~selectively~~ hybridizable to any of the isolated variants of the allele of a human kappa opioid receptor gene of claim 31 ~~30~~ under high stringency hybridization conditions, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and wherein the nucleic acid molecule is at least 90% homologous with the variant nucleotide sequence.
46. (currently amended) The unicellular host of either of Claims 44 or 45, wherein said host ~~comprises~~ is selected from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, R1.1, B-W, L-M, COS1, COS7, BSC1, BSC40, BMT10 ~~or~~ and Sf9 cells.
47. (withdrawn) A method for determining a susceptibility in a subject to at least one physiological response, condition or disease related to the endogenous opioid system, nociception, neurotransmitter release endogenous opioid system, learning, memory and cognition; cocaine, amphetamine and other stimulants self-administration; behavioral sensitization to cocaine, opiates, alcohol and tobacco; opiate, amphetamine and alcohol withdrawal, physical dependence and tolerance; neuroendocrine function, reproductive function, prolactin regulation, stress

responsivity; physiology and pathology of mood and affect; immune function, and gastrointestinal function, comprising the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human kappa opioid receptor gene;
- b) determining whether said human kappa opioid receptor gene of said first allele comprises a variant allele of claim 30, such that the presence of said at least one variation in said human kappa opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to at least one said physiological response, condition or disease relative to the susceptibility to said at least one said physiological response, condition or disease in a standard.

48. (withdrawn) The method for determining a susceptibility to at least one addictive disease of Claim 47, further comprising the step of determining whether said human kappa opioid receptor gene of said second allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G36T, A843G, C846T, C852T, C948T, or C1008T, or any combination thereof, such that the presence of said at least one variation in said human kappa opioid receptor gene of said second allele is expected to be indicative of the subject's susceptibility to said at least one physiological response, condition or disease relative to the susceptibility to said at least one physiological response, condition or disease in said standard.
49. (withdrawn) The method of Claim 48 wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
50. (withdrawn) A method for determining a susceptibility to pain in a subject relative to a susceptibility of pain in a standard, wherein the method comprises the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human kappa opioid receptor gene;
- b) determining whether said human kappa opioid receptor gene of said first allele comprises a DNA sequence of claim 30, such that the presence of said at least one variation in said human kappa opioid receptor gene of said first allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said first allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

51. (withdrawn) The method of Claim 50 for determining a susceptibility to pain in a subject, further comprising the step of determining whether said second allele of said bodily sample comprises a human kappa opioid receptor gene comprising a variant allele of claim 30, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility of pain in said standard, wherein said second allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

52. (withdrawn) A method for determining a therapeutically effective amount of pain reliever to administer to a subject in order to induce analgesia in said subject relative to a therapeutically effective amount of pain reliever to administer to a standard in order to induce analgesia in said standard, wherein the method comprises determining a susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein susceptibility to pain in said subject is expected to be indicative of said therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject relative to said therapeutically effective amount of pain reliever to administer to said standard to induce analgesia in said standard.

53. (withdrawn) The method of Claim 52 for determining a therapeutically effective amount of pain reliever to administer to said subject, wherein determining susceptibility to pain in said subject comprises the steps of:
- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human kappa opioid receptor gene; and
 - b) determining whether said first allele comprises a human kappa opioid receptor gene of claim 30, wherein the presence of said at least one variation in said human kappa opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to pain relative to said susceptibility of pain in said standard, wherein said first allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, such that said therapeutically effective amount of pain reliever to administer to the subject in order to induce analgesia is related to said susceptibility to pain in said subject relative to susceptibility to pain in said standard.
54. (withdrawn) The method of Claim 53, wherein determining susceptibility to pain in said subject relative to susceptibility to pain in said standard further comprises the step of determining whether said second allele of said bodily sample from said subject comprises a human kappa opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises G36T, A843G, C846T, C852T, C948T, or C1008T, or any combination thereof, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said second allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, and the therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject is related to the presence of said at least one variation in said human kappa opioid receptor gene of said second allele of said bodily sample from said subject.

55. (withdrawn) A method for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from at least one addictive disease to treat the at least one addictive disease in said subject relative to a therapeutically effective amount of therapeutic agent to administer to a standard suffering from the at least one addictive disease to treat the at least one addictive disease in said standard, wherein the method comprises the steps of:
- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human kappa opioid receptor gene; and
 - b) determining whether said first allele comprises a human kappa opioid receptor gene comprising a variant allele of claim 30,
- wherein the presence of said at least one variation in said human kappa opioid receptor gene of said first allele is expected to be indicative of the therapeutically effective amount of said therapeutic agent to administer to the subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said first allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.
56. (withdrawn) The method of Claim 55 for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from said at least one addictive disease to treat said at least one addictive disease, relative to said therapeutically effective amount of said therapeutic agent administered to said standard suffering from said at least one addictive disease to treat said at least one addictive disease in said standard, further comprising the step of determining whether said second allele of said bodily sample from said subject comprises a human kappa opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G36T, A843G, C846T, C852T, C948T, or C1008T, or any combination thereof, such that the

presence of said at least one variation in said second allele related to said therapeutically effective amount of said therapeutic agent administered to said subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said second allele of said standard comprises a human kappa opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

- 57. (withdrawn) The method of either of Claims 55 or 56, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbiturate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
- 58. (canceled)
- 59. (canceled)